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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,648	09/15/2005	Gregor Sagner	21810-US	2235

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EXAMINER	
STRZELECKA, TERESA E	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
08/19/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)
	10/549,648	SAGNER ET AL.
	Examiner	Art Unit
	TERESA E. STRZELECKA	1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☒ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 1, 2011 has been entered.

2. Claims 15-17 were previously pending. Applicants amended claim 15 and added new claim 18. Claims 15-18 will be examined.

3. Applicants' amendments overcame all of the previously presented rejections. This office action contains new grounds for rejection necessitated by amendment.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wittwer et al. (US 7,081,226 B1, filed June 4, 1997), King et al. (US2004/0014202 A1; cited in the previous office action), Lee et al. (Biotechniques, vol. 27, pp. 342-349, 1999; cited in the IDS and in the previous office action), Wittwer-2 et al. (Methods, vol. 25, pp. 430-442, 2001; cited in the IDS and in the previous office action), Amirkhanian et al. (U.S. Patent No. 6,870,165 B2; cited in the previous office action) and Belfer (U.S. Patent No. 5,563,588 A; cited in the previous office action).

A) Regarding claim 15, Wittwer et al. teach a real-time PCR instrument comprising:

an excitation unit comprising:

- a rotating carousel comprising at least 24 reaction vessels containing a reaction mixture, wherein said reaction vessels are positioned in a monitoring position in that fluorescence excitation and monitoring are performed along the same axis of the positioned reaction vessel (Fig. 11, Fig. 19 H-I, Fig. 20, Fig. 21, Fig. 28; col. 31, lines 8-67; col. 32, lines 29-67; col. 33, lines 43-58; col. 39, lines 30-55),

- a single light source capable of emitting light toward the reaction vessels (col. 29, lines 63-66; col. 31, lines 1-7),

- a detection unit comprising at least 5 separate fluorescent detector entities, each of said detector entities having a central detection wavelength, said wavelengths being distinct from each other by at least 25 nm (col. 32, lines 29-49, where Wittwer et al. teach that three or more colors can be analyzed), and

- means for heating and cooling (Fig. 8; col. 33, lines 8-42).

Regarding claim 16, Wittwer et al. teach capillaries (Fig. 19; Fig. 20; Fig. 21).

Regarding claim 17, Wittwer et al. teach detection wavelengths selected from an interval between 500-800 nm in 20 nm bins (col. 32, lines 64-66).

Regarding claim 18, Wittwer et al. teach glass capillaries with an outer diameter of less than 5 mm (col. 34, lines 5-63).

B) Wittwer et al. do not teach the following limitations:

- a lightpipe being arranged for receiving light from the reaction vessel and capable of distributing homogeneously said light into optical fiber bundles, wherein the light does not pass through a wavelength excluding device prior to being distributed into said optical fiber bundles,

- a plurality of at least 5 optical fiber bundles, each said bundle being arranged for receiving homogeneously distributed light from the lightpipe, and transmitting said light to said fluorescent detector entities,

C) Regarding claim 15, King et al. teach a real time PCR instrument comprising:

- an excitation unit comprising:

- at least 1 light source capable of emitting light toward a reaction vessel containing fluorescent compounds (Fig. 1; page 1, [0004]-[0007]),

- a lightpipe being arranged for receiving light from the reaction vessel and capable of distributing homogeneously said light for transmission to optical fiber bundles (Fig. 1; Fig. 6a, 7, 8; page 1, [0008]; page 2, [0023], claim 19, 20; page 4, [0043], [0044]);

- a detection unit comprising at least 5 separate fluorescent detector entities, each of said detector entities having a central detection wavelength, said wavelengths being distinct from each other by at least 25 nm (page 1, [0009]; Fig. 4; Fig. 6b, c; Fig. 8; page 3, [0031]-[0032], claims 27, 28);

- a plurality of at least 5 optical fiber bundles, each said bundle being arranged for receiving homogeneously distributed light from the lightpipe, and transmitting said light to said fluorescent detector entities (page 4, [0043]), and

- means for heating and cooling (Fig. 1; page 2, [0023]-[0024]).

Regarding claim 16, King et al. teach a single light source (page 1, [0007]).

D) King et al. teach multiple detection units and detection of at least four different fluorophores, but do not specifically teach at least 5 fluorescent detectors and central detection wavelengths separated by at least 25 nm.

E) Regarding claims 15-17, Lee et al. teach detection of seven different fluorophores in a multiplex PCR reaction, with the emission wavelengths differing by at least 25 nm from each other (page 342, first paragraph; Table 3; page 344, third paragraph; Fig. 1).

Regarding claims 15-17, Wittwer-2 et al. teach that multiplexing of real-time PCR can be achieved by introducing additional fluorescent dyes into a reaction and using fluorophores with well-spaced emission maxima, as well as an instrument where separate detectors are used to detect each of the fluorophores, with bandpass filter ranges encompassing the emission maxima of the fluorophores (page 434, last paragraph; Table 3; page 435, first paragraph; page 436, last paragraph; Fig. 3, 4; page 437).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have incorporated the suggestions of Lee et al. and Wittwer-2 et al. into the system of real-time PCR of Wittwer et al. and King et al. with a reasonable expectation of success. Wittwer et al. teach that detection of at least three fluorophores, if desired, is possible. King et al. already teach multiple light sources and detector units. Wittwer-2 et al. provide a solution of how detection of more than four fluorophores, such as the seven cited by Lee et al., can be achieved (page 437, last paragraph):

"Even with array analysis of emitted light, variable excitation may be needed when more than three or four colors are used. For example, on one commercial platform, only three colors could be distinguished in real time, but up to seven colors were resolved when the excitation wavelength was scanned with an off-line synchronous scanning fluorometer (37). The prototype instrument shown in Fig. 4 has variable excitation. That is, different excitation wavelengths can be selected by adjusting the monochromator. By interrogating at multiple wavelengths, different fluorophores can be optimally excited. This means that two or more resonance energy transfer donors can be excited in the same tube, each transferring to multiple acceptors (probe/probe and primer/probe formats)."

The motivation to use more fluorophores in the reactions is provided be Lee et al., who state (page 349, second paragraph):

"A multiplex PCR system has the advantages of increased sample throughput and potential cost savings. Our example provides good results for a multiplex, end-point SNP analyses. The excellent spectral discrimination suggests that additional reporter dyes could be added at shorter wavelengths without toss in spectral resolution."

F) None of the references teach an arrangement where the light does not pass through a wavelength excluding device prior to being distributed into optical fiber bundles.

G) However, optical detection systems which do not contain a wavelength excluding device between the light source and the fiber optic bundles were known in the art at the time of the invention.

Belfer teaches a system for distributing light from a light source into separate fiber bundles without the use of wavelength excluding devices (Fig. 3-5, 7, 9; col. 1, lines 45-53; col. 2, lines 31-39; col. 4, lines 32-47).

Amirkhanian et al. teach multi-color multiplexing optical detection system where no wavelength excluding devices are placed between the light source and optical fiber bundles (Fig. 1, 3; col. 3, lines 30-45).

It would have been *prima facie* obvious to one of ordinary skill in the art to use alternative configurations of light source-fiber optic bundles-detector system without wavelength-excluding devices as described by Belfer and Amirkhanian et al. in the device of Wittwer et al., King et al., Lee et al. and Wittwer-2 et al. King et al. suggests a system configuration without wavelength-excluding devices (page 3, [0035]), but without providing any detail of such arrangement. One of skill in the art would realize that removing wavelength-excluding devices would result in increasing light intensity traveling through the fiber optic bundles, increasing detection sensitivity.

7. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TERESA E STRZELECKA
Primary Examiner
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August 15, 2011